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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/886,964	06/21/2001	Ya Fang Liu	YFLU-P02-001	6742
23628	7590	10/30/2003	EXAMINER	
WOLF GREENFIELD & SACKS, PC FEDERAL RESERVE PLAZA 600 ATLANTIC AVENUE BOSTON, MA 02210-2211			WEBER, JON P	
			ART UNIT	PAPER NUMBER
			1651	

DATE MAILED: 10/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/886,964	LIU, YA FANG	
	Examiner	Art Unit	
	Jon P Weber, Ph.D.	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 April 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 36,39,40,43 and 44 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 36,39,40,43 and 44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

Status of the Claims

The response with amendments filed 25 August 2003 has been received and entered. Claims 36, 39, 40, 43 and 44 have now been presented for examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 36, 39, 40, 43 and 44 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is argued that while no specific inhibitors are presented, a method of identifying inhibitors of MLK enzymes is presented and following these procedures, inhibitors can be identified. It is urged that once inhibitors are found the disclosure teaches how they can be used to treat Parkinson's.

The screening assay itself is not in contention. A screening assay only needs the possibility of finding an inhibitor to be enabled. Thousands of compounds might be unsuccessfully screened for an inhibitor yet the screen itself would still be fully enabled. That is, one could practice the screen albeit unsuccessfully.

Thus, the availability of a screen is no guarantee of success in finding an inhibitor for an enzyme. It is the subject of considerable original research to provide such inhibitors. The

experimentation is undue and not merely routine when the decisions on which compounds to test are not guided by the disclosure. In the instant case, there is no guidance at all on the selection of suitable test compounds. Thus no inhibitor leads are provided and the screening assay constitutes a wish to know as opposed to clear guidance. This is not the basis of sound enablement.

Even assuming, *in arguendo*, that the screening assay would provide inhibitors of MLK enzymes, the disclosure does not enable the use of the putative inhibitors to treat Parkinson's so as to prevent neuronal cell death. The disclosure merely speculates that inhibitors, if they were available, could be used to treat Parkinson's. Since there are no working examples of treatment with even a model system with inhibitors of MLK enzymes, it cannot be seen how the disclosure could enable such treatment in vivo. Inventions targeted for human therapy bear a heavy responsibility to provide supporting evidence because of the unpredictability in biological responses to therapeutic treatments. The standard of enablement is higher for such inventions because effective treatments for disease conditions are relatively rare, and may be unbelievable in the absence of strong supporting evidence. Claims drawn to pharmaceutically acceptable compositions and to methods of administering compounds to humans generally require supporting evidence because of the unpredictability in biological responses to therapeutic treatments. The instant specification is absent actual working examples of how the invention would treat an individual with Parkinson's let alone prevent neuronal cell death in a patient so afflicted.

Applicant's arguments filed 25 August 2003 have been fully considered but they are not persuasive. The rejection under 35 U.S.C. 112, first paragraph is adhered to for the reasons of record and the additional reasons above.

Claim Rejections - 35 USC § 103

Claims 36, 39, 40, 43 and 44 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. (US 6,060,247).

It is argued that Parkinson's is only mentioned in the background in passing and then only to state that apoptosis occurs in Parkinson's. It is urged that there is no linkage between inhibiting MLK activity and treating Parkinson's.

The reference to Parkinson's in column 1 is not a casual one with respect to apoptosis as urged in the response. Rather, Parkinson's is a neurodegenerative disease identified as having a substantive undesired apoptosis component in the course of the disease. One of the purposes of Miller et al. is to identify compounds that inhibit apoptosis in neurons (column 2, lines 30-48). Compounds identified by the screening method are said to decrease cell death and therefore have therapeutic value in treating neurodegenerative diseases (column 7, lines 31-34). It is clearly disclosed that the screening assays can be performed with constructs for mixed lineage kinases (MLK) (column 29, line 41 to column 30, line 9). Hence, contrary to the argument in the response, there is linkage between treating neurodegenerative disorders involving abnormal apoptosis such as Parkinson's and screened inhibitors of MLK enzymes.

Applicant's arguments filed 25 August 2003ly considered but they are not persuasive. The rejection under 35 U.S.C. 103 adhered to for the reasons of record and the additional reasons above.

No claims are allowed.

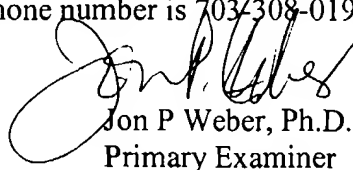
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon P Weber, Ph.D. whose telephone number is 703-308-4015. The examiner can normally be reached on daily, off 1st Fri, 9/5/4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 703-308-4743. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Jon P Weber, Ph.D.
Primary Examiner
Art Unit 1651

JPW
29 October 2003